

REMARKS

Applicants respectively cancel Claims 8-9, and 12-17 to simplify the prosecution process of this application and expedite it for allowance. Claims 7, and 10-11 are pending.

Election/Restriction:

In the Office Action dated February 9, 2006, the Examiner has set forth a requirement for restriction under 35 U. S. C. § 121. By Applicants' Response on March 8, 2008, Group II Claims 7-13 with amendment to Claim 7 was selected. Claim 7 was previously amended to depend from Claim 1 as same method, the independent claim of Group I. As previously submitted, the groups I and II should be properly examined together.

Claim Objections

In the Office Action dated March 28, 2006, the Examiner rejected Claim 7 stating that it recites non-elected inventions. In a telephone conference, the Office indicated that Claims 7-13 were examined and withdrawal of this objection is proper. Applicants respectfully submit that Groups I and II are the same subject matter, both related to a method of modulating differentiation of oligodendrocytes; therefore, Groups I and II should be examined together. Applicants cancel claims 8-9, 12 and 14-17 to expedite the prosecution process for allowance.

Claim Rejection Under 35 U.S.C. § 112

In the Office Action dated March 28, 2006, the Examiner rejected Claims 7-13 stating that Claims 7-13 fail to comply with the enablement requirement and the claim(s) contains subject matter which was not described in the specification in a way to enable one skilled in the art to which it pertains to make and/or use the invention. The Examiner stated that the method claimed is absent of supporting evidence because relevant literature reports the use of osteopontin (OPN) in opposite manner for the same purpose, i.e. inducing oligodendrocyte differentiation and enhancing remyelination by increasing exposure of oligodendrocyte precursor cells to OPN (Selvaraju et al, Mol. Cell. Neurosci., 2004, Vol. 25, pp 707-721). The Examiner further stated Selvaraju et al teach that in mixed cortical cultures, recombinant

OPN treatment stimulates myelin sheath formation. Applicants respectively traverse this rejection.

Applicants respectfully cancel Claims 8-9 and 12-13, thus, the rejection with respect to these claims is rendered moot.

Applicants reviewed the reference cited by the Examiner and respectfully disagree with the Examiner's conclusion that the teaching of Selvaraju et al conflict with the biological process that Applicants teach in this application. The conclusion from Selvaraju et al is not applicable because of the following reasons:

- a. Applicants use primary normal rat oligodendrocyte progenitors from neonatal rats. Selvaraju et al used CG4 (rat) and Oli-neu (mouse) cell lines that are not normal, not oligodendrocyte progenitors, and not representative of primary oligodendrocytes phenotypically or functionally. Therefore, it is not proper to conclude that Selvaraju et al taught a method of inducing differentiation of primary oligodendrocyte precursor cells and enhancing remyelination by increasing exposure of oligodendrocyte precursor cells to OPN.
- b. Applicants show osteopontin (OPN) drives migration of primary oligodendrocyte progenitors from neonatal rats *in vitro*, Selvaraju et al never showed proliferation, migration or differentiation of purified oligodendrocyte progenitors in response to OPN.
- c. Applicants show OPN by immunohistochemistry, *in situ* hybridization, TaqMan in normal rat spinal cord in neurons, in rat stroke brain in the infarct, and in rat lyssolecithin treated demyelinating/remyelinating spinal cord in inflammatory macrophages/microglia. Selvaraju et al taught the presence of OPN in cuprizone fed mice in neurons of the brain stem by double-labeling immunohistochemistry, but no staining of oligodendrocytes or progenitors in the white matter corpus callosum; Selvaraju et al. taught staining of astrocytes, macrophages and microglia in cuprizone fed mice. Applicants use a different demyelinating and remyelinating model than Selvaraju et al did and concentrated on spinal cord while Selvaraju et al looked in brain.

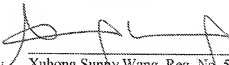
In summary, i) Applicants use purified oligodendrocyte precursor cells and a different demyelinating and remyelinating model than Selvaraju et al did; ii) Applicants provide an

experimental result that shows increasing of oligodendrocyte precursor cells at a remyelination site to OPN to enhance oligodendrocyte precursor cells at the site, and then reducing exposure of oligodendrocyte precursor cells to OPN at said site would enhance differentiation of said oligodendrocyte precursor cells into oligodendrocytes and enhance remyelination; and iii) Selvaraju et al used different cell types, CG4 (rat) and Oli-ncu (mouse) cell lines, that are not normal, not oligodendrocyte progenitors, and not representative of primary oligodendrocytes phenotypically or functionally. Thus, the conclusion from their experiments should not be taken as the evidence against Applicants' results and claims in this application.

Applicants respectfully cancel claims 8-9 and 12-13 to simplify and expedite the prosecution process, and Applicants reserve the right to file one or more continuation or divisional applications directed to above subject matter.

In view of the present amendment and remarks. The Applicants submit that the claims, as amended, are in condition for allowance, and respectfully request early, favorable action on the application. Should the Examiner believe that an interview would advance the prosecution of this application, the Applicants invite him to contact the undersigned at 908.231.3648.

Respectfully submitted,



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